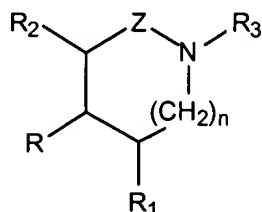


## IN THE CLAIMS

1 (currently amended). A compound of the formula:



wherein

Z is  $-\text{C}(\text{R}_{18})(\text{R}_{19})-$  wherein  $\text{R}_{18}$  and  $\text{R}_{19}$  are hydrogen;

n is 0;

R is  $-(\text{CH}_2)_m-\text{W}$  wherein m is 0 and W is  $-\text{C}(\text{O})_2-\text{G}$  wherein G is hydrogen;

$\text{R}_1$  and  $\text{R}_2$  are independently selected from the group consisting of loweralkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxyalkyl, alkoxyalkoxyalkyl, thioalkoxyalkoxyalkyl, cycloalkyl, cycloalkylalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, aminocarbonylalkenyl, alkylaminocarbonylalkenyl, dialkylaminocarbonylalkenyl, hydroxyalkenyl, aryl, arylalkyl, aryloxyalkyl, arylalkoxyalkyl, (N-alkanoyl-N-alkyl)aminoalkyl, alkylsulfonylamidoalkyl, heterocyclic, (heterocyclic)alkyl and  $(\text{R}_{aa})(\text{R}_{bb})\text{N}-\text{R}_{cc}-$  wherein  $\text{R}_{aa}$  is aryl or arylalkyl,  $\text{R}_{bb}$  is hydrogen or alkanoyl and  $\text{R}_{cc}$  is alkylene; and

$\text{R}_3$  is  $\text{R}_4-\text{C}(\text{O})-\text{R}_5-$  wherein  $\text{R}_5$  is alkylene and  $\text{R}_4$  is selected from the group consisting of

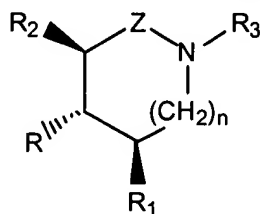
(i)  $(\text{R}_{11})(\text{R}_{12})\text{N}-$  wherein  $\text{R}_{11}$  is hydrogen and  $\text{R}_{12}$  is selected from the group consisting of arylalkyl, and diarylalkyl

and

(ii)  $(\text{R}_{11a})(\text{R}_{12a})\text{N}-\text{N}(\text{H})-$  wherein  $\text{R}_{11a}$  and  $\text{R}_{12a}$  are independently selected from the group consisting of aryl and alkyl;

or a pharmaceutically acceptable salt thereof.

21 (currently amended). The A compound according to claim 1 of the formula:



wherein

Z is -C(R<sub>18</sub>)(R<sub>19</sub>)- wherein R<sub>18</sub> and R<sub>19</sub> are hydrogen;

n is 0;

R is -(CH<sub>2</sub>)<sub>m</sub>-W wherein m is 0 and W is -C(O)<sub>2</sub>-G wherein G is hydrogen;

R<sub>1</sub> and R<sub>2</sub> are independently selected from the group consisting of loweralkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxycarbonylalkyl, hydroxyalkyl, haloalkyl, haloalkoxyalkyl, alkoxyalkoxyalkyl, thioalkoxyalkoxyalkyl, cycloalkyl, cycloalkylalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, aminocarbonylalkenyl, alkylaminocarbonylalkenyl, dialkylaminocarbonylalkenyl, hydroxyalkenyl, aryl, arylalkyl, aryloxyalkyl, arylalkoxyalkyl, (N-alkanoyl-N-alkyl)aminoalkyl, alkylsulfonylamidoalkyl, heterocyclic, (heterocyclic)alkyl and (R<sub>aa</sub>)(R<sub>bb</sub>)N-R<sub>cc</sub>- wherein R<sub>aa</sub> is aryl or arylalkyl, R<sub>bb</sub> is hydrogen or alkanoyl and R<sub>cc</sub> is alkylene; and

R<sub>3</sub> is R<sub>4</sub>-C(O)-R<sub>5</sub>- wherein R<sub>5</sub> is alkylene and R<sub>4</sub> is selected from the group consisting of

(i) (R<sub>11</sub>)(R<sub>12</sub>)N- wherein R<sub>11</sub> is hydrogen and R<sub>12</sub> is diarylalkyl

and

(ii) (R<sub>11a</sub>)(R<sub>12a</sub>)N-N(H)- wherein R<sub>11a</sub> and R<sub>12a</sub> are independently selected from the group consisting of aryl and alkyl;

or a pharmaceutically acceptable salt thereof.

157 (currently amended). The compound according to claim 1 wherein R<sub>1</sub> is aryl substituted with one substituent selected from the group consisting of methoxy, methoxyethoxy, and isopropoxyethoxy; R<sub>2</sub> is 1,3-benzodiox-5-yl; R<sub>5</sub> is methylene; and

~~R<sub>12</sub> is selected from the group consisting of arylalkyl and diarylalkyl wherein each aryl group of the diarylalkyl is substituted with methyl or ethyl.~~

158 (currently amended). The compound according to claim 1 wherein R<sub>1</sub> is phenyl substituted with one substituent selected from the group consisting of methoxy, methoxyethoxy, and isopropoxyethoxy; R<sub>2</sub> is 1,3-benzodiox-5-yl; R<sub>5</sub> is methylene; and ~~R<sub>12</sub> is selected from the group consisting of phenylalkyl and diphenylalkyl wherein each phenyl group of the diphenylalkyl is substituted with methyl or ethyl.~~

159 (currently amended). The compound according to claim 21 wherein R<sub>1</sub> is aryl substituted with one substituent selected from the group consisting of methoxy, methoxyethoxy, and isopropoxyethoxy; R<sub>2</sub> is 1,3-benzodiox-5-yl; R<sub>5</sub> is methylene; and ~~R<sub>12</sub> is selected from the group consisting of arylalkyl and diarylalkyl wherein each aryl group of the diarylalkyl is substituted with methyl or ethyl.~~

160 (currently amended). The compound according to claim 21 wherein R<sub>1</sub> is phenyl substituted with one substituent selected from the group consisting of methoxy, methoxyethoxy, and isopropoxyethoxy; R<sub>2</sub> is 1,3-benzodiox-5-yl; R<sub>5</sub> is methylene; and ~~R<sub>12</sub> is selected from the group consisting of phenylalkyl and diphenylalkyl wherein each phenyl group of the diphenylalkyl is substituted with methyl or ethyl.~~

161 (previously presented). A compound selected from the group consisting of  
trans, trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N-((bis-o-tolyl)methyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid,  
trans, trans-2-(4-(2-methoxyethoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N-(2,2-dimethyl-1-phenylpropyl)-1-aminocarbonylmethyl)pyrrolidine-3-carboxylic acid,  
trans, trans-2-(4-(2-methoxyethoxy)phenyl)-4-(1,3-benzodioxol-5-yl)-1-(N-((bis-o-tolyl)methyl)amino)carbonylmethyl)pyrrolidine-3-carboxylic acid,  
trans, trans-2-(4-(2-isopropoxyethoxy)phenyl)-4-(1,3-benzodioxol-5-yl)-1-(N-(2,2-dimethyl-1-phenylpropyl)-1-amino)carbonylmethyl)pyrrolidine-3-carboxylic acid,  
trans, trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N-(3,3-dimethyl-1-phenylbutyl)-1-amino)carbonylmethyl)pyrrolidine-3-carboxylic acid,

trans, trans-2-(4-(2-isopropoxyethoxy)phenyl)-4-(1,3-benzodioxol-5-yl)-1-(N-((1-o-toulyl)-1-(o-ethylphenyl)methyl)amino)carbonylmethyl)pyrrolidine-3-carboxylic acid, trans, trans-2-(4-(2-(2-propoxy)ethoxy)phenyl)-4-(1,3-benzodioxol-5-yl)-1-(N-phenyl-N-t-butylhydrazinocarbonylmethyl)pyrrolidine-3-carboxylic acid, and trans, trans-2-(4-(2-methoxyethoxy)phenyl)-4-(1,3-benzodioxol-5-yl)-1-(N-phenyl-N-t-butylhydrazinocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

162 (new). A pharmaceutical composition for antagonizing endothelin comprising a therapeutically effective amount of trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

163 (new). A pharmaceutical composition for treating cancer comprising a therapeutically effective amount of trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

164 (new). A pharmaceutical composition for treating prostate cancer comprising a therapeutically effective amount of trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

165 (new). A pharmaceutical composition for treating nociception comprising a therapeutically effective amount of trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

166 (new). A pharmaceutical composition for treating bone pain associated

with bone cancer comprising a therapeutically effective amount of trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)-pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

167 (new). A method for antagonizing endothelin comprising administering to a mammal in need of such treatment a therapeutically effective amount of trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)-pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

168 (new). A method for treating cancer comprising administering to a mammal in need of such treatment a therapeutically effective amount of trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)-pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

169 (new). A method for treating prostate cancer comprising administering to a mammal in need of such treatment a therapeutically effective amount of trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)-pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

170 (new). A method for treating nociception comprising administering to a mammal in need of such treatment a therapeutically effective amount of trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)-pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

171 (new). A method for treating bone pain associated with bone cancer comprising administering to a mammal in need of such treatment a therapeutically effective amount of trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

172 (new). A method for antagonizing endothelin comprising administering to a mammal in need of such treatment a pharmaceutical composition comprising a therapeutically effective amount of trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

173 (new). A method for treating cancer comprising administering to a mammal in need of such treatment a pharmaceutical composition comprising a therapeutically effective amount of trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

174 (new). A method for treating prostate cancer comprising administering to a mammal in need of such treatment a pharmaceutical composition comprising a therapeutically effective amount of trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

175 (new). A method for treating nociception comprising administering to a mammal in need of such treatment a pharmaceutical composition comprising a therapeutically effective amount of trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

176 (new). A method for treating bone pain associated with bone cancer comprising administering to a mammal in need of such treatment a pharmaceutical composition comprising a therapeutically effective amount of trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)-pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

177 (new). A pharmaceutical composition for antagonizing endothelin comprising a therapeutically effective amount of (2R,3R,4S)-(+)-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

178 (new). A pharmaceutical composition for treating cancer comprising a therapeutically effective amount of (2R,3R,4S)-(+)-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

179 (new). A pharmaceutical composition for treating prostate cancer comprising a therapeutically effective amount of (2R,3R,4S)-(+)-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

180 (new). A pharmaceutical composition for treating nociception comprising a therapeutically effective amount of (2R,3R,4S)-(+)-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

181 (new). A pharmaceutical composition for treating bone pain associated with bone cancer comprising a therapeutically effective amount of (2R,3R,4S)-(+)-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

182 (new). A method for antagonizing endothelin comprising administering to a

mammal in need of such treatment a therapeutically effective amount of (2R,3R,4S)-(+)-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)-pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

183 (new). A method for treating cancer comprising administering to a mammal in need of such treatment a therapeutically effective amount of (2R,3R,4S)-(+)-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)-pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

184 (new). A method for treating prostate cancer comprising administering to a mammal in need of such treatment a therapeutically effective amount of (2R,3R,4S)-(+)-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)-pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

185 (new). A method for treating nociception comprising administering to a mammal in need of such treatment a therapeutically effective amount of (2R,3R,4S)-(+)-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)-pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

186 (new). A method for treating bone pain associated with bone cancer comprising administering to a mammal in need of such treatment a therapeutically effective amount of (2R,3R,4S)-(+)-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

187 (new). A method for antagonizing endothelin comprising administering to a mammal in need of such treatment a pharmaceutical composition comprising a



therapeutically effective amount of (2R,3R,4S)-(+)-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

188 (new). A method for treating cancer comprising administering to a mammal in need of such treatment a pharmaceutical composition comprising a therapeutically effective amount of (2R,3R,4S)-(+)-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

189 (new). A method for treating prostate cancer comprising administering to a mammal in need of such treatment a pharmaceutical composition comprising a therapeutically effective amount of (2R,3R,4S)-(+)-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

190 (new). A method for treating nociception comprising administering to a mammal in need of such treatment a pharmaceutical composition comprising a therapeutically effective amount of (2R,3R,4S)-(+)-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.

191 (new). A method for treating bone pain associated with bone cancer comprising administering to a mammal in need of such treatment a pharmaceutical composition comprising a therapeutically effective amount of (2R,3R,4S)-(+)-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.